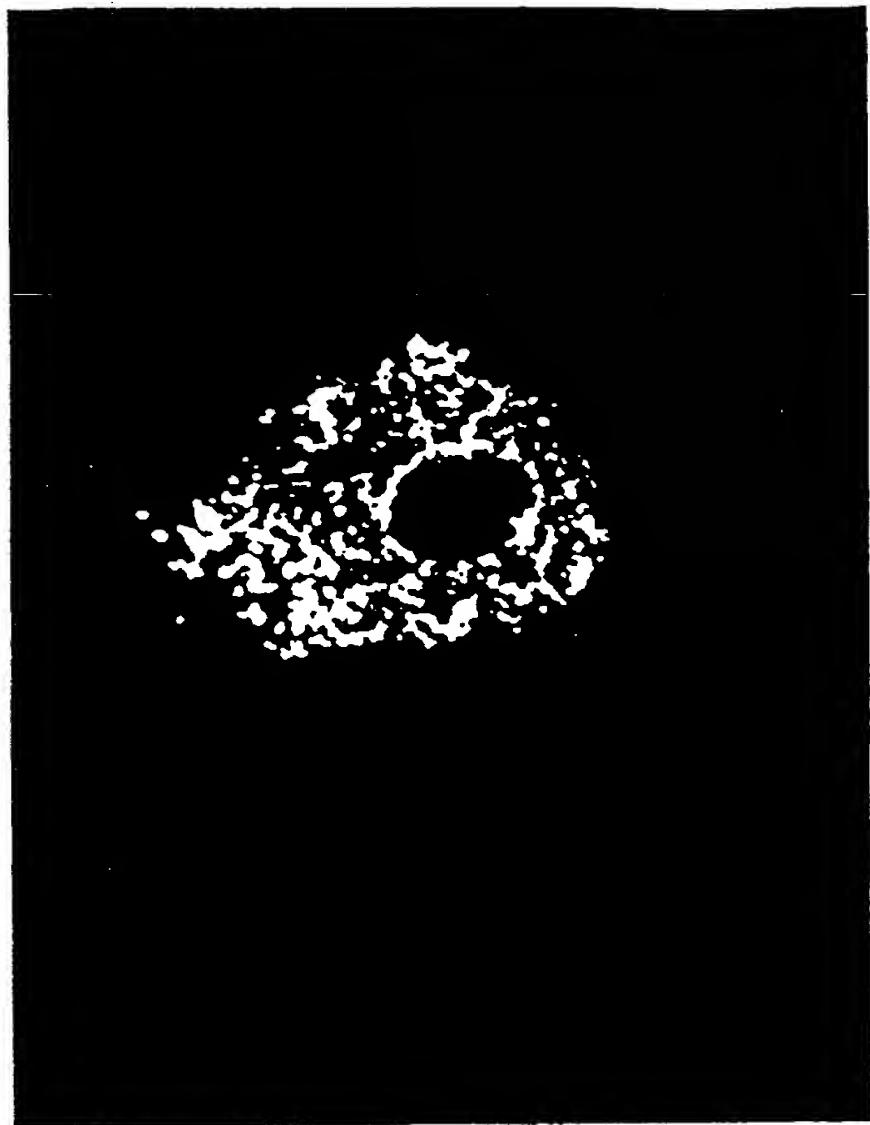


09/831720

WO 00/28947

1/7

PCT/FR99/02761



00000000000000000000000000000000

Analysis by confocal microscopy using the antibody 8D7
of the mitochondrial localization of the PBR receptor
on keratinocytes A431 (green coloration).

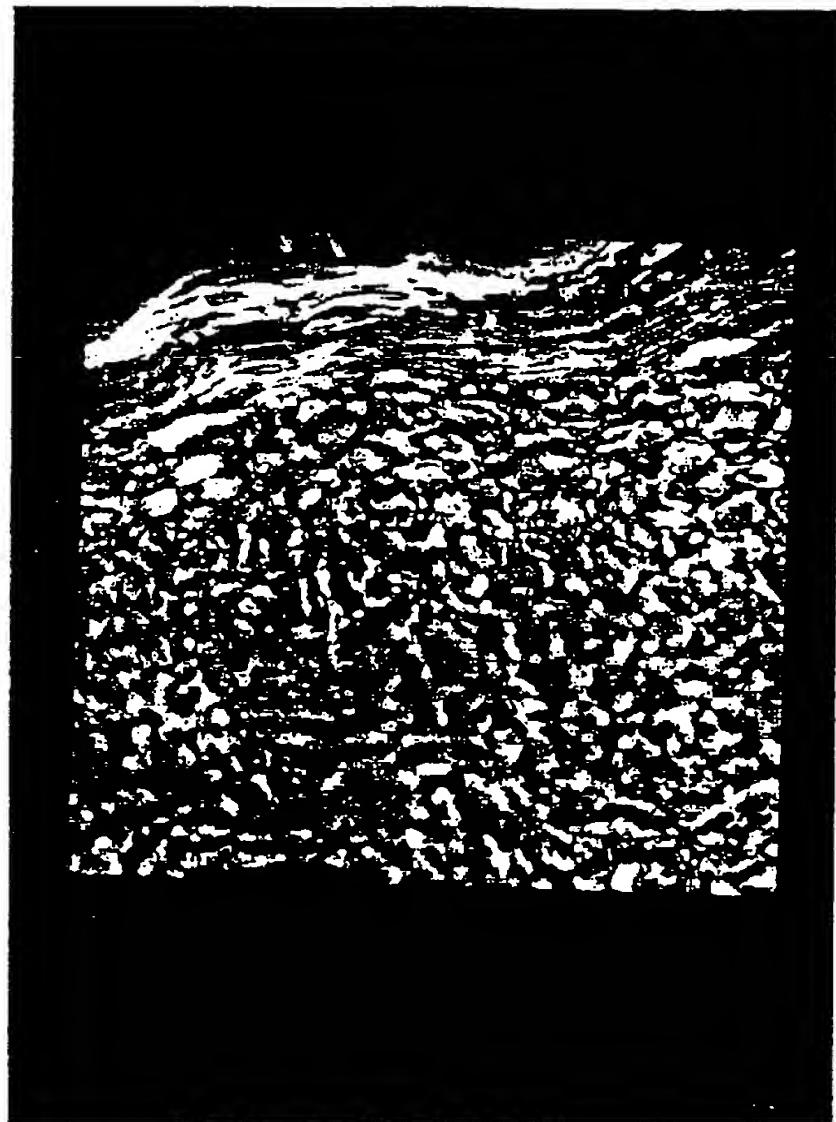
FIGURE 1

09/831720

WO 00/28947

2/7

PCT/FR99/02761



The immunohistological analysis performed on a section of normal human epidermis reveals an expression of PBR which increases from the *stratum basale* to the *stratum corneum* (red coloration).

FIGURE 2

09/831720

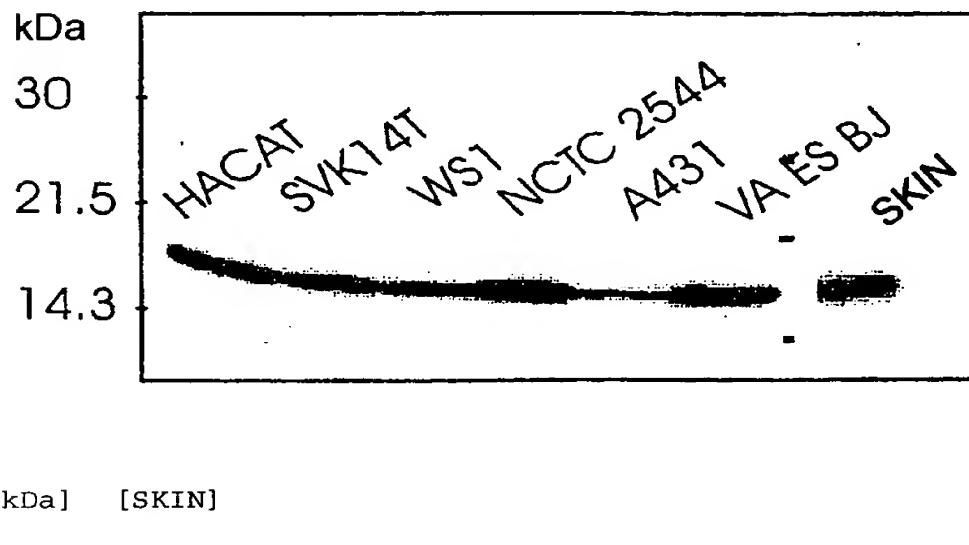
WO 00/28947

3/7

PCT/FR99/02761

Expression of PBR on keratinocyte lines
and on normal human skin lines:

Western blot analysis



[kDa] [SKIN]

8D7 antibody labeling (1 µg/ml final)

The deposits are normalized by assaying the total
proteins of the lysate:
deposits for each line 30 µg

FIGURE 3

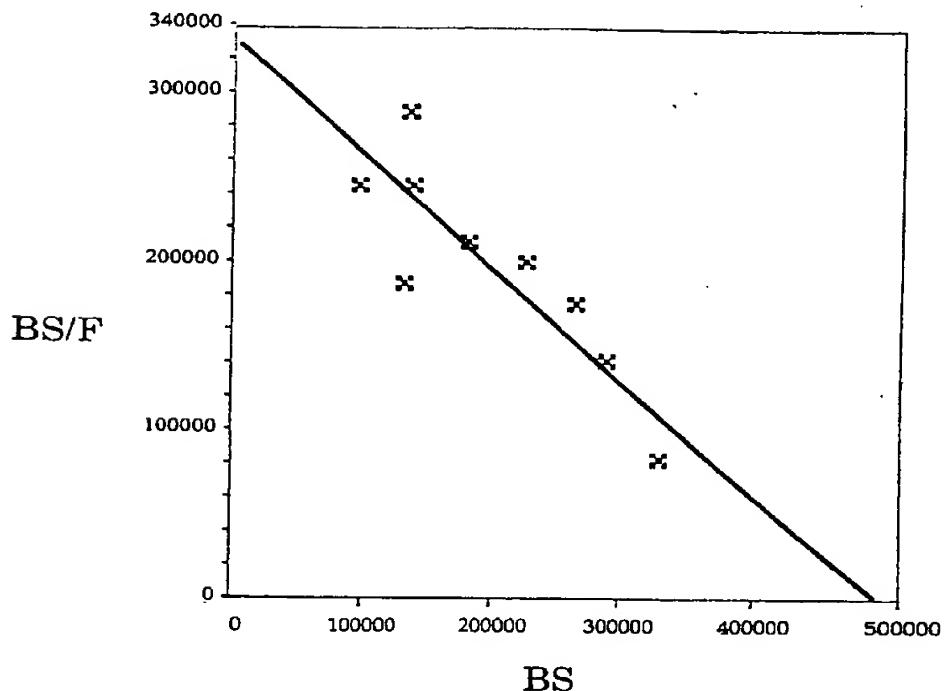
09/831720

WO 00/28947

4/7

PCT/FR99/02761

Scatchard study
on keratinocytes A431



B max = 472 000 ± 68 000 receptors/cell

KD = 1.5 ± 0.3 mM

FIGURE 4

09/831720

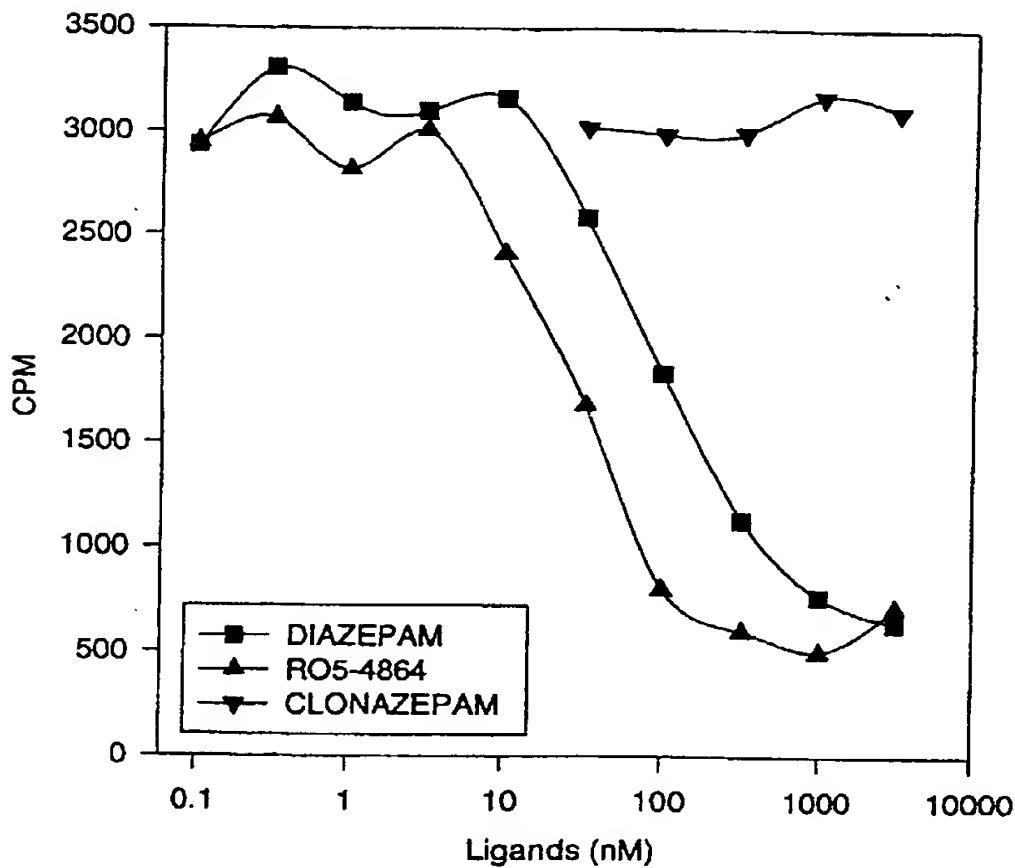
WO 00/28947 PCT/FR99/02761

WO 00/28947

5/7

PCT/FR99/02761

Pharmacological profile of ligands for PBR
on keratinocytes A431



Curve of displacement of the reference ligand
[³H]-PK11195 by Ro 5-4864 (peripheral ligand),
clonazepam (central ligand) and
diazepam (mixed ligand)

FIGURE 5

09/831720

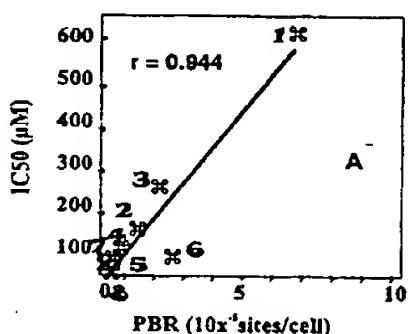
FRANCAIS - VERSOIS FRANCAIS

WO 00/28947

6/7

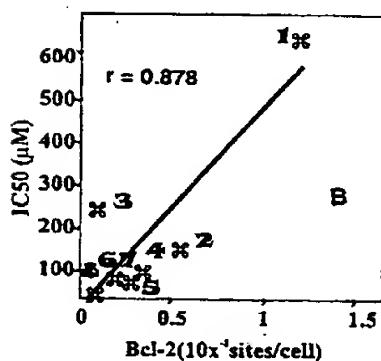
PCT/FR99/02761

Involvement of PBR in the protection of hematopoietic cells against damage caused by oxygenated radicals

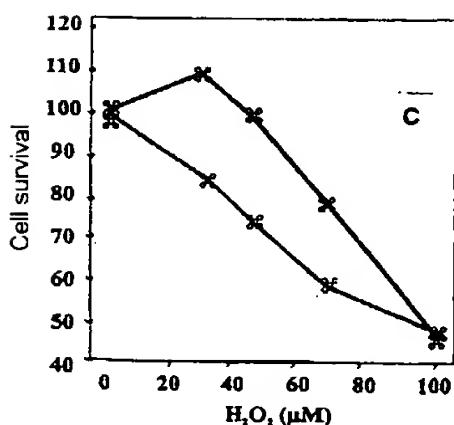


Correlation between the level of expression PBR [A] and of Bcl-2 [B] and of resistance to the toxicity of H₂O₂

1 = THP₁ 2 = U937 3 = K562
IM9 5 = CEM 6 = NALM-6
7 = Jurkat 8 = RAJI



The H₂O₂ concentrations which induce 50% toxicity after incubation for 24 h [IC₅₀] are expressed as a function of the number of PBR or Bcl-2 sites.



Viability of wild-type Jurkat cells and of cells transfected with PBR with respect to H₂O₂ toxicity after incubation for 24 h

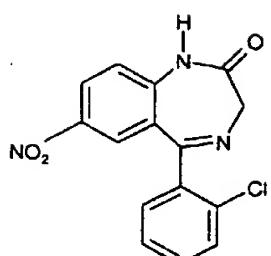
FIGURE 6

09/831720

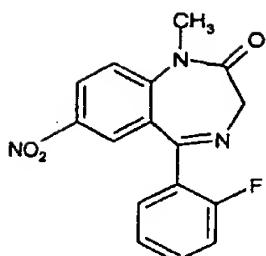
WO 00/28947

7/7

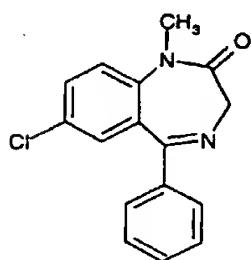
PCT/FR99/02761



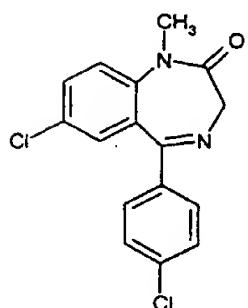
CLONAZEPAM



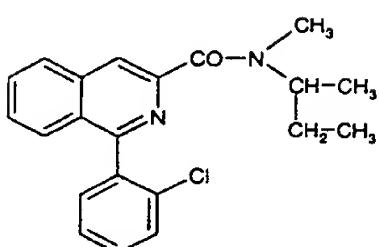
FLUNITRAZEPAM



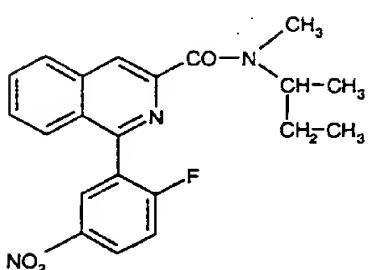
DIAZEPAM
Ro 5-2807



CHLORODIAZEPAM
Ro 5-4864



PK 11195



PK 14105

TOP SECRET - DEFENSE EDITION

Main ligands for the central and peripheral
benzodiazepine receptors

FIGURE 7